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Patient's perception of exacerbations of COPD—the PERCEIVE study ☆

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Summary
The evaluation of therapies requires the development of patient-reported outcomes (PROs) that help clinicians to understanding the symptoms, perceptions and feelings of patients with exacerbations of chronic obstructive pulmonary disease (COPD).
With the aim of obtaining information on the perceptions of patients with COPD, their exacerbations and expectations of treatment, a random telephone contact survey in six countries was performed.
From 83,592 households screened, 1100 subjects with symptoms compatible with COPD were identified. The most frequent symptom was shortness of breath (78%). The most frequent complaint was that due to their COPD: ''they could not complete the activities they like to do'' (54%); 17% (187) of individuals were afraid that their COPD would cripple, or eventually kill them. Exacerbations generated a mean of 5.1 medical visits/year (SD = 4.6) with the mean duration of exacerbation symptoms being 10.5 days. Increased coughing was the exacerbation symptom having the strongest impact on well-being (42%). Fifty-five percent of patients declared that quicker symptom relief was the most desired requirement for treatment.
New data are provided on the impact of COPD and its exacerbations on the daily life of patients. These data will help to develop PROs designed to evaluate the effectiveness of different therapies for exacerbated COPD.

Abbreviations: COPD, chronic obstructive pulmonary disease; GOLD, global initiative for chronic obstructive lung disease; PRO, patient-reported outcome

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common cause of morbidity and mortality in developed countries. The age-adjusted mortality rate from COPD doubled from 1970 to 2002 in the United States, whereas rates from stroke and heart disease decreased by 63% and 52% respectively.[1]

COPD represents a large economic burden to society. The mean annual direct medical costs of a patient with COPD in Spain have been quantified as $1876[2] and up to $10,812 for severe patients in the USA.[3] In all studies, between 35% and 45% of the costs derived from the attention to exacerbations, particularly the most severe that require hospital admission.[2–5] Patients with COPD, followed in observational studies in primary care, have about two exacerbations per year,[6] and exacerbations accelerate the rate of decline of pulmonary function[7] and significantly impair the quality of life of COPD patients, both short-[8,9] and long-term.[10,11] Because of the lack of validated specific questionnaires to investigate the impact of exacerbations on well-being, quantification of the impact of exacerbations on quality of life has been performed using the same generic and specific questionnaires used for long-term study of patients in stable state.[12–14] The evaluation of therapies for exacerbations of COPD requires outcomes focused on the patient. A more comprehensive knowledge of the symptoms, perceptions and feelings of patients with exacerbations of COPD is required to develop patient-reported outcomes (PROs) taking into account the patient's perceptions of the positive and negative aspects of antibiotics and other treatments.[15]

This survey was designed to obtain information on patients' perception of their COPD, their exacerbations and their expectations about treatment. To date, most COPD studies are based on interviews with patients recruited through their treatment centers, which has the advantage of confirmed COPD status, but the disadvantage of highly clustered and related cases, as well as a bias risk towards the more compliant patients under certain influence of the present therapy. This study targeted a regionally highly scattered and completely independent sample, facing the challenge of motivation as well as correct screening. To collect information from a large sample of individuals in a reasonable time frame, an international telephone interview was designed.

Method

Subject selection

The PERCEIVE study (perception of exacerbations of chronic obstructive pulmonary disease) is a survey performed by Psyma International Medical Marketing Research GmbH (Rueckersdorf/Nuernberg, Germany) using computer-assisted telephone interviewing (CATI) in six countries, using native speakers in the respective regional main languages: Germany, France, Italy, Spain, the UK and the USA. Participation in the survey was voluntary, confidential and anonymous. In these countries, between 92% and 97% of the households have telephones. This assumes that approximately 5% to 7% of households can only be reached by cellular phones, probably those comprising younger people (less relevant to the target group).

The initial sampling technique was a regionally stratified, fully representative aleatory household contact, based on existing complete phone data records. To be eligible for the survey, participants had to be older than 18 years and to respond affirmatively to several screening questions: "During the last 12 months, which of the following symptoms have you suffered from (prompted list of 9 symptoms)?" affirming at least one of the following:

(a) "shortness of breath for months to years",
(b) "cough that produces green mucus" and
(c) "frequent respiratory infections that worsen symptoms".

Additionally, respondents only qualified if they confirmed:

(d) "Have you had 3 months of mucus production during each of the last two consecutive years?" and
(e) "During the last 12 months have you taken medication for respiratory problems?" (excluding asthma) .

A pilot phase in Germany and the UK, demonstrated that the initial frequency of households with a suspected COPD household member was approximately 4% in Germany and approximately 3% in the UK. The mentioned screening process used reduced the household incidence to a figure of around 1% in both countries. This differs from the COPD prevalence rate of 4–10% reported in the literature.[16,17]

This design required $n = 1100$ interviews across all 6 countries. This allows equal sample precision in the population estimates with an error of 5% and a power of 80% for a population prevalence of the different respiratory symptoms of at least 5%, thereby making the global sample representative of each of the countries.

Collection of data

Telephone interviews were carried out by previously trained interviewers between 09:00 and 22:00 on workdays. The interview lasted about 15 min. The survey questionnaire (available from the authors on request) was based on 29 'closed' questions with additional rating scales. The questionnaire was developed for this survey and pre-tested. The impact of COPD on daily life activities was investigated by reading to the patient a list of 10 activities and asking whether or not COPD influenced them. Similarly, the impact of flare-ups on daily life was investigated using a list of 6 activities. Feelings about exacerbations were analyzed by asking the individuals to score each of 7 sentences on a scale from 1 to 10, where 1 was equal to "did not make any difference to my wellbeing" and 10 was equal to "made life a great deal more difficult". Finally, the importance of each individual symptom of exacerbation on wellbeing was investigated again with a score system from 1 to 10, where 1 was equal to "did not make any difference to my wellbeing" and 10 was equal to "made life a great more difficult". Results are presented as the percentage of individuals responding from 8 to 10. Expectations about treatment of exacerbations were investigated by asking the

patient to choose from a list of 6 items the most needed in the treatment of exacerbations.

Statistical analysis

A descriptive analysis was made using frequency tables for the nominal variables and measures of central trends and dispersion for the continuous variables. The χ^2 test was used to analyze the relationship between categorical variables. The Student's *t*-test was used for continuous variables that were normally distributed and where indicated, non-parametric tests were used. All statistical tests were two-sided and comparisons with a probability of error $<5\%$ were considered significant. Tests were adjusted using the Bonferroni Correction for multiple comparisons.

Results

Characteristics of the population

To reach the required number of interviews, a total of 131,990 telephone contacts were necessary to identify 83,592 eligible individuals. Of these, 3073 (3.6%) provided incomplete or inconsistent data. Among the rest, 79,419 did not have chronic respiratory symptoms so were not included. Ultimately, 1100 (1.37%) questionnaires were completed (Fig. 1).

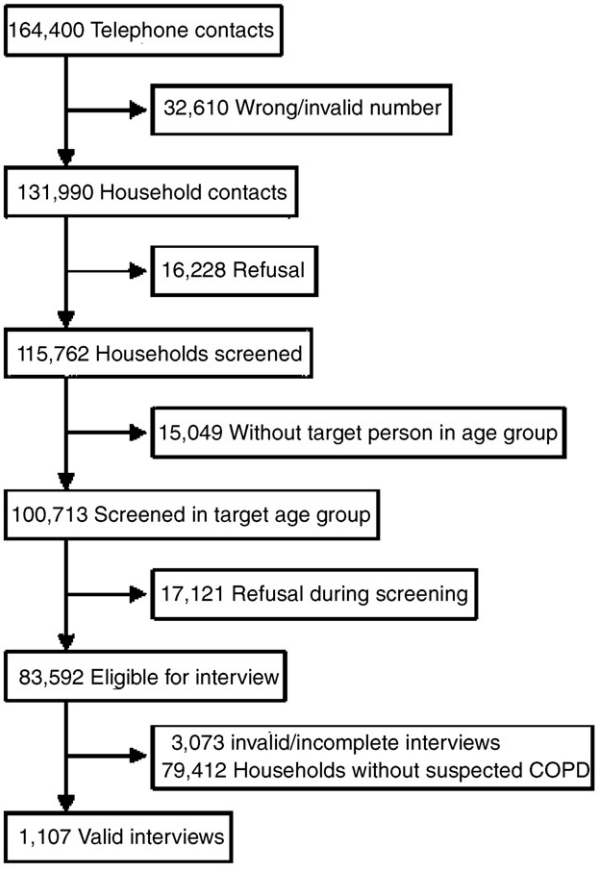

Figure 1 Disposition of the survey population.

The clinical and demographical characteristics of the individuals surveyed are presented in Table 1. More than half of the respondents were more than 50 years old; 61% were female and up to 58% had a significant associated disease. The most frequently reported symptom was shortness of breath (78%), followed by cough and production of green mucus (71%), wheezing was reported by as many as 47% of participants (Fig. 2).

Impact of COPD on daily life activities

Up to 17% (187) individuals answered that they were afraid that the disease would cripple them or would eventually kill them ('scared patients'), 46% declared that it was a serious disease that they can control with medication ('serious patients') and only 34% answered that it was mainly a nuisance but not too serious ('nuisance patients'). Differences in characteristics between these three groups are presented in Table 1.

Patients were asked about 10 different situations or activities of daily life that potentially could be affected by COPD. The most frequent answers were that due to COPD: "they could not complete the activities they like to do" (596; 54%) and "they suffer from sleep disturbances" (569; 52%) (Fig. 3).

Frequency and characteristics of exacerbations

A total of 736 (89%) patients declared that they had suffered at least one episode of 'flare-up' of symptoms during the previous year. Of these, 89% needed to see their doctor due to these episodes and 21% were admitted to the hospital. Exacerbations generated a mean of 5.1 visits to the doctor per patient per year (SD = 4.6). Mean duration of symptoms of exacerbation was 10.5 days. Frequency and duration of flare ups increased markedly with age: the duration of flare-ups among those between 40 and 60 years was 9.8 days (mean; SD = 10.2 days), it increased dramatically to 14.4 days (SD = 20.5 days) among those over 60.

Impact of exacerbations of COPD on daily-life activities

Figure 4 shows the percentage of individuals with the highest scores,[8–10] meaning "made life a great deal more difficult". Increased coughing was mentioned by 42% of respondents as having a strong impact on wellbeing, followed by increasing shortness of breath (37%), fatigue (37%) and increased production of sputum (35%) (Fig. 4).

During an exacerbation, only 41% declared that they could continue with their normal life while increasing their usual medication. Up to 45% had to stay in bed or in couch all day, and 24% of the whole group or 55% of those who worked had to stop working due to the exacerbations.

Another set of questions referred to their feelings in relation to exacerbations. Noteably, for strong impact of exacerbations on mood, 30% were frightened of the onset of winter, 27% wanted to be alone or only with few close friends or family, 22% were very scared of exacerbations and up to 27% felt very frustrated with themselves.

Table 1 Characteristics of the population surveyed according to self-reported impact of COPD.

	All ($n = 1100$)	'Scared patients' ($n = 191$)	'Serious patients' ($n = 502$)	'Nuisance patients' ($n = 377$)
Gender, male %	39	40	38	40
Age, yrs (51+)	51%	65%	53%††	39%*,§
Duration of symptoms, yrs (SD)	13.7 (12.3)	16.8 (13.4)	14.6 (13.0)	11.1 (9.8)*,§
Years since diagnosis (SD)	10.4 (10.4)	12.9 (12.0)	11.0 (11.2)	8.4 (7.7)*,§
Smoking, %				
Yes	36	31	34	42††
No	35	32	34	37
Ex-smokers	28	37	30	20*,**
Co-morbidity, %				
Sleep disturbances	24	30	25	19†
Cardiac diseases/hypertension	20	32	21**	13*,**
Chronic pain	16	23	18	12†,***
Arthritis	16	23	17	12†
Depression/anxiety	13	23	12**	8*
Diabetes	6	11	6	3†
Other	16	24	16††	12†
None	42	28	38††	54*,§
Employment, %				
Part-time	12	9	16	10
Full-time	31	16	29*	41*,**
Unemployed	10	14	7††	13††
Homemaker	10	9	11	10
Retired	33	51	33*	22*,§
Missing	3	1	3	3
Education, %				
University level	21	14	21	27
Preparatory school	24	21	25	24
High school	39	51	39††	33*
Discontinued high school	10	8	9	11
Missing	6	6	7	5

Results are based on two-sided tests. For each significant pair, the key of the category with the smaller column proportion appears under the category with the larger column proportion.
Tests are adjusted for all pair comparisons within a row of each innermost sub-table using the Bonferroni Correction.
*$P<0.001$ in the comparison with 'scared patients'.
†$P<0.01$ in the comparison with 'scared patients'.
††$P<0.05$ in the comparison with 'serious patients'.
§$P<0.001$ in the comparison with 'serious patients'.
**$P<0.01$ in the comparison with 'serious patients'.
***$P<0.05$ in the comparison with 'serious patients'.

Expectations about treatment of exacerbations of COPD

Treatments administered for exacerbations are shown in Fig. 5. Antibiotics were prescribed to 66% of individuals, 54% received a mucolytic and only 26% received a course of oral corticosteroids. After presenting a list of 6 items regarding expectations about treatment, 55% of patients stated that quicker symptom relief was the most desired requirement of treatment, followed by longer periods between flare-ups (40%) and fewer side effects (36%) (Fig. 6).

Discussion

This survey provides new data on the impact of COPD and its exacerbations on patient's daily life. Such data are often not collected in clinical or epidemiological studies despite being highly relevant to the understanding of how patients feel about their disease and their expectations with treatment. In addition, there is a growing interest in patient-centered care, which requires assessment of patient values, concerns and preferences. This information is crucial for the development of PROs aimed at evaluating the effectiveness of different therapies for stable and exacerbated COPD.

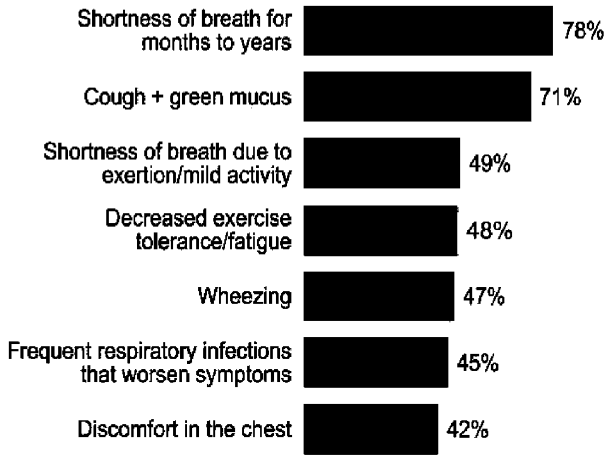

Figure 2 Symptoms most frequently reported by survey respondents.

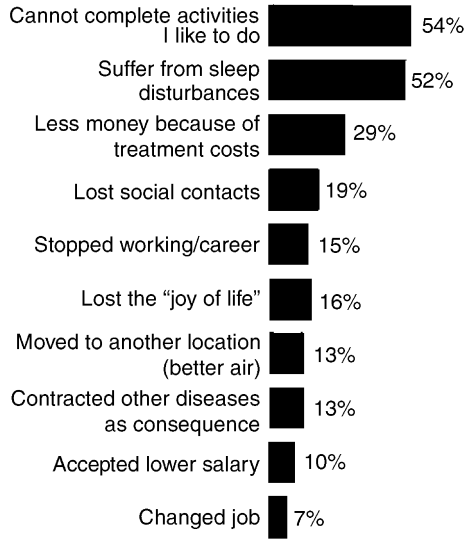

Figure 3 Proportion of daily life activities affected by COPD reported by survey respondents.

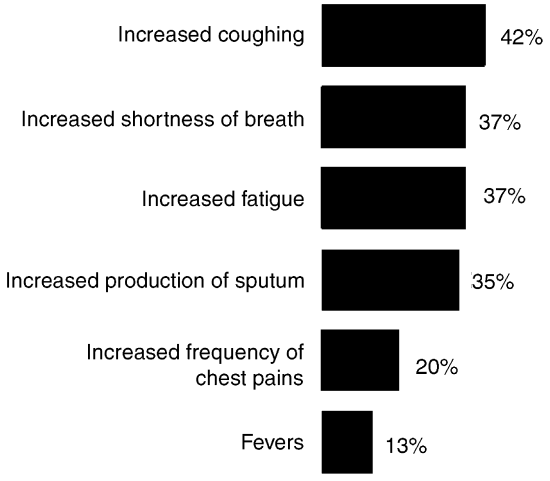

Figure 4 Percentage of survey respondents reporting symptoms with a high impact on wellbeing.

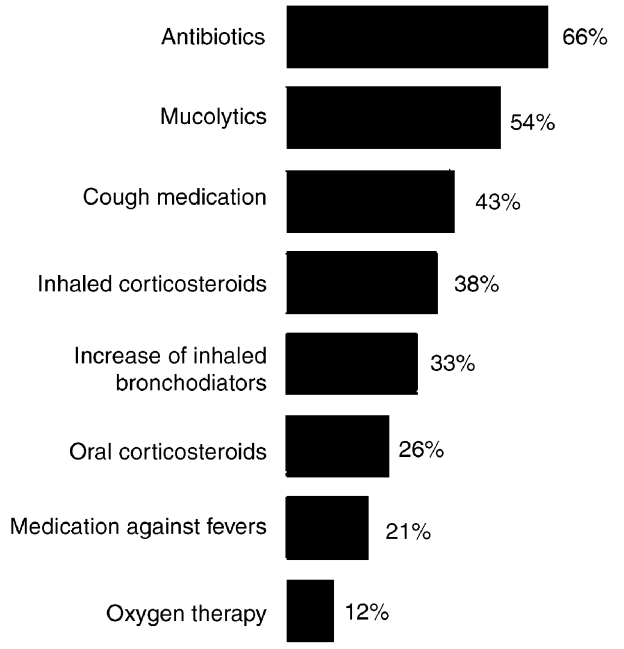

Figure 5 Treatments received for exacerbations of COPD in the survey respondents.

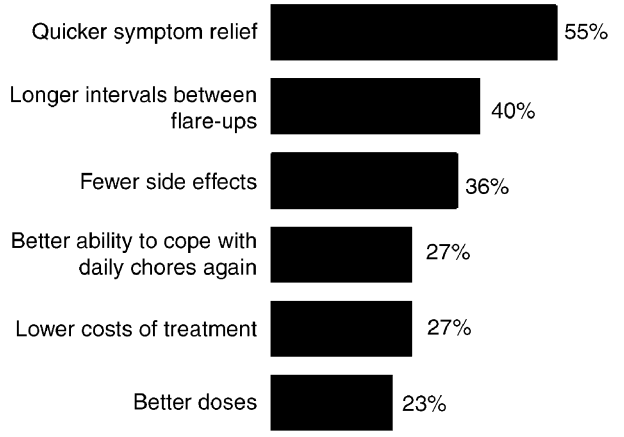

Figure 6 Ideal characteristics of a COPD therapy as listed by survey respondents.

The impact of COPD and its exacerbations on the disease in the daily life of respondents is considerable. Up to 17% responded that they were afraid that the disease would cripple them or eventually kill them. These individuals were older, with a longer duration of the disease, more co-morbidities and a higher proportion of ex-smokers. The 34% who responded that the disease was only a nuisance were significantly younger, with shorter duration of symptoms, fewer co-morbidities and a higher proportion of active smokers. This last group probably represented the milder form of the disease. However, it is important to point out that some of these patients may have moderate or severe disease. A similar international telephone survey showed that patients tend to underestimate their morbidity. There was a significant disparity between subjects' perception of

disease severity and the degree of severity indicated by an objective breathlessness scale.[18] These results emphasize the importance of PROs in addition to physiological measurements to evaluate the results of therapies.

The most important aspect of COPD from the patient's perspective is the effect on normal daily life activities. This negative effect increases during exacerbations, because up to 45% of individuals had to stay in bed or in couch all day during the episodes. This is consistent with another study that showed that symptoms were less important from the patient's perspective than the impact of exacerbations on daily life[19] or on health status.[11,12,20] Patients with COPD are markedly inactive in daily life compared with individuals of the same age group[21] and this inactivity is accentuated significantly during exacerbations.[22] Furthermore, patients with frequent exacerbations are more likely to become housebound.[22] Strategies aimed at increasing physical activity and preventing exacerbations may improve outcomes in COPD, since time spent outdoors is significantly associated with improved health status,[22] high levels of physical activity have a preventive effect on readmissions[23] and reducing the frequency of severe exacerbations and admissions may improve survival.[24]

The patients interviewed generated a mean of 5 visits to the doctor for exacerbations in the previous year and 21% of them were admitted to hospital. A recent survey also demonstrated a mean self-reported frequency of exacerbations of 4.6 episodes per year.[19] Clinical trials consistently observed a lower frequency of exacerbations, indicating that patients included in clinical trials may not represent the whole population of COPD,[25] or patients may have different perceptions than physicians about what constitutes an exacerbation, underlining the importance of PROs. A further example of the differences between patients' and physicians' perceptions is the duration of exacerbations. This study showed a mean duration of 10.5 days, extended to 14.4 days in individuals older than 60 years. Similarly, in another survey the mean duration was 12.7 days, ranging from 1 to 119 days.[19] However, when data are collected by the investigators, mean recovery time ranges from 5 to 8 days.[26,27] In fact, exacerbations defined by changes in individual symptoms, as experienced by the patients, are only weakly related to event-based exacerbations, as perceived by the physician.[28]

Exacerbations had a strong influence on mood. A significant proportion of respondents wanted to be alone and felt very frustrated with themselves during exacerbations, which ties in with findings that COPD patients experience significantly more psychological distress, particularly depression than the general population.[29] From our results it can be hypothesized that frequent exacerbations might be one of the main causes of this distress.

It is important to note that more than a half of respondents wished to receive treatments that provide quicker relief of symptoms of exacerbations and also for treatments that prolong periods between flare-ups. These should be the two main goals of treatment, to prevent exacerbations, but when this is not possible, to treat quickly. Baseline treatment of COPD aims to reduce the frequency of exacerbations, but the choice of antibiotic in infective exacerbations may result in shorter duration of symptoms[26,30] and in prolonged time between episodes.[31] The knowledge of the expectations of patients tells us what really matters to them and offers a new perspective in the design of outcomes for clinical trials.

The survey has been performed using telephone interviews. The strengths and weaknesses of this sampling method have been extensively described elsewhere.[18,32] A possible limitation could be the availability of telephone lines, but more than 90% of the households in the countries surveyed have telephones. It is also likely that elderly subjects residing in chronic care facilities were undersampled and finally, this sampling method does not permit verification of self-reported information. On the other hand, telephone sampling permits non-clustered sampling of units, eliminates interviewer control over sample selection and provides anonymity for the respondent.[18]

One of the difficulties of telephone sampling is the large number of calls required to obtain an adequate sample. In our study, more than 100,000 attempts were required to obtain 1100 valid interviews, results similar to other telephone surveys.[18] These 1100 interviews represented 1.37% of the screened individuals, percentage that is very similar to the self-reported prevalence of COPD obtained by a random postal survey in a population of the same age group in a recent study in the UK.[33] As the diagnosis of COPD cannot be verified in such a survey, questions on chronic respiratory symptoms and the use of respiratory medications, excluding asthma, as surrogate of spirometric diagnosis of COPD were included. The requirement of a positive response to all three screening questions could have provided a more restrictive criterion of COPD; however, to be included in the survey individuals had to have declared to suffer from chronic bronchitis and have taken respiratory medications during the last 12 months in addtion to a positive response to at least one of the screening questions. The age was not restricted to those older than 40 or 50, to permit assessment of GOLD 0 individuals and a recent international survey showed that up to 11.8% of subjects aged between 20 and 44 years have GOLD 0 COPD.[34] In our sample, 35% of individuals were non-smokers, which is consistent with other epidemiological studies of COPD.[16,35] Although it is not clear if non-smokers identified in epidemiological studies or population-based surveys are really affected by COPD or other chronic respiratory disease,[36–38] no existing consensus exclude non-smokers from the COPD definition so far[39,40] and the inclusion of non-smokers should not affect the objectives and results of our study.

In summary, this study provides new data about the impact of COPD and its exacerbations on daily life of patients. These new data will help to understand patient's perception of their disease and their expectations with treatment. These data are crucial for the development of PROs aimed at evaluating the effectiveness of different therapies for stable and exacerbated COPD.

References

1. Jemal A, Ward E, Hao Y, Thun M. Trends in the leading causes of death in the United States, 1970–2002. *J Am Med Assoc* 2005;**294**:1255–9.

2. Miravitlles M, Murio C, Guerrero T, Gisbert R. On behalf of the DAFNE study group. costs of chronic bronchitis and COPD: a one year follow-up study. *Chest* 2003;**123**:784–91.
3. Hilleman DE, Dewan N, Malesker M, Friedman M. Pharmacoeconomic evaluation of COPD. *Chest* 2000;**118**:1278–85.
4. Andersson F, Borg S, Jansson S-A, et al. The costs of exacerbations in chronic obstructive pulmonary disease (COPD). *Respir Med* 2002;**96**:700–8.
5. Masa JF, Sobradillo V, Villasante C, Jiménez-Ruiz CA, Fernández-Fau L, Viejo JL, et al. Costs of chronic obstructive pulmonary disease in Spain: estimation from a population-based study. *Arch Bronconeumol* 2004;**40**:72–9.
6. Miravitlles M, Mayordomo C, Artés M, Sánchez-Agudo L, Nicolau F, Segú JL, On behalf of the EOLO Group. Treatment of chronic obstructive pulmonary disease and its exacerbations in general practice. *Respir Med* 1999;**93**:173–9.
7. Donaldson GC, Seemungal TAR, Bhomik A, Wedzicha JA. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax* 2002;**57**:847–52.
8. Doll H, Grey-Amante P, Duprat-Lomon I, Sagnier PP, Thate-Waschke I, Lorenz J, et al. Quality of life in acute exacerbations of chronic bronchitis: results from a German population study. *Resp Med* 2002;**96**:39–51.
9. Aaron SD, Vandemheen KL, Clinch JJ, Ahuja J, Brison RJ, Dickinson G, et al. Measurment of short-term changes in dyspnoea and disease-specific quality of life following an acute COPD exacerbation. *Chest* 2002;**121**:688–96.
10. Seemungal TAR, Donaldson GC, Paul EA, Bestall JC, Jeffries DJ, Wedzicha JA. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998;**157**:1418–22.
11. Miravitlles M, Ferrer M, Pont A, Zalacain R, Alvarez-Sala JL, Masa JF, et al. For the IMPAC study group. exacerbations impair quality of life in patients with chronic obstructive pulmonary disease: a two-year follow-up study. *Thorax* 2004;**59**:387–95.
12. Doll H, Miravitlles M. Quality of life in acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease: a review of the literature. *Pharmacoeconomics* 2005;**23**:345–63.
13. Doll H, Duprat-Lomon I, Ammerman E, Sagnier PP. Validity of the St. George's respiratory questionnaire at acute exacerbation of chronic bronchitis: comparison with the Nottingham health profile. *Qual Life Res* 2003;**12**:117–32.
14. Schulman, Ronca, and Bucuvalas, Inc. Confronting COPD in America. Available at: http://www.lungusa.org/site/apps/s/content.asp?c=dvLUK9O0E&b=34706&ct=67262. Accessed Feb 24, 2006.
15. Pechère JC. Patients' interviews and misuse of antibiotics. *Clin Infect Dis* 2001;**33**(Suppl 3):S170–3.
16. Sobradillo Pena V, Miravitlles M, Gabriel R, Jiménez-Ruiz CA, Villasante C, Masa JF, et al. Geographical variations in prevalence and underdiagnosis of COPD: results of the IBERPOC multicentre epidemiological study. *Chest* 2000;**118**:981–9.
17. Halbert RJ, Isonaka S, George D, Iqbal A. Interpreting COPD prevalence estimates. What is the true burden of disease? *Chest* 2003;**123**:1684–92.
18. Rennard S, Decramer M, Calverley PM, et al. Impact of COPD in North America and Europe in 2000: subjects' perspective of confronting COPD international survey. *Eur Respir J* 2002;**20**:799–805.
19. Haughney J, Partridge MR, Vogelmeier C, Larsson T, Kessler R, Stahl E. Exacerbations of COPD: quantifying the patient's perspective using discrete choice modelling. *Eur Respir J* 2005;**26**:623–9.
20. Miravitlles M, Calle M, Alvarez-Gutierrez F, Gobartt E, López F, Martín A, The EIME Group. Exacerbations, hospital admissions and impaired health status in chronic obstructive pulmonary disease. *Qual Life Res* 2006;**15**:471–80.
21. Pitta F, Troosters T, Spruit MA, Probst VS, Decramer M, Gosselink R. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2005;**171**:972–7.
22. Donaldson GC, Wilkinson TMA, Hurst JR, Perera WR, Wedzicha JA. Exacerbations and time spent outdoors in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2005;**171**:446–52.
23. Garcia-Aymerich J, Farrero E, Félez MA, Izquierdo J, Marrades RM, Antó JM. Risk factors of readmission to hospital for a COPD exacerbation: a prospective study. *Thorax* 2003;**58**:100–5.
24. Soler-Cataluña JJ, Martínez-García MA, Sánchez PR, Salcedo E, Navarro M, Ochando R. Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. *Thorax* 2005;**60**:925–31.
25. Herland K, Akselsen JP, Skjonsberg OH, Bjermer L. How representative are clinical study patients with asthma or COPD for a larger "real life" population of patients with obstructive lung disease? *Respir Med* 2005;**99**:11–9.
26. Miravitlles M, Zalacain R, Murio C, Alvarez-Sala JL, Masa JF, Verea H, et al. On behalf of the IMPAC study group. speed of recovery from acute exacerbations of COPD after treatment with antimicrobials: results of a two-year study. *Clin Drug Invest* 2003;**23**:439–50.
27. Seemungal TAR, Donaldson GC, Bhowmik A, Jeffries DJ, Wedzicha JA. Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000;**161**:1608–13.
28. Calverley P, Pauwels R, Löfdahl CG, Svensson K, Higenbottam T, Carlsson LG. Relationship between respiratory symptoms and medical treatment in exacerbations of COPD. *Eur Respir J* 2005;**26**:406–13.
29. Wagena EJ, Arrindell WA, Wouters EFM, van Schayck CP. Are patients with COPD psychologically distressed? *Eur Respir J* 2005;**26**:242–8.
30. Miravitlles M, Llor C, Naberan K, Cots JM, Molina J. Variables associated with recovery from acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease. *Respir Med* 2005;**99**:955–65.
31. Wilson R, Jones P, Schaberg T, Arvis P, Duprat-Lomon I, Sagnier PP. Antibiotic treatment and factors influencing short and long term outcomes of acute exacerbations of chronic bronchitis. *Thorax* 2006;**61**:337–42.
32. Potthoff RF. Telephone sampling in epidemiologic research: to reap the benefits, avoid the pitfalls. *Am J Epidemiol* 1994;**139**:967–78.
33. Iversen L, Hannaford PC, Price DB, Godden DJ. Is living in a rural area good for your respiratory health? results from a cross-sectional study in Scotland. *Chest* 2005;**128**:2059–67.
34. De Marco R, Accordini S, Cerveri I, Corsico A, Sunyer J, Neukirch F. An international survey of chronic obstructive pulmonary disease in young adults according to GOLD stages. *Thorax* 2004;**59**:120–5.
35. Coultas DB, Mapel D, Gagnon R, Lydick E. The health impact of undiagnosed airflow obstruction in a national sample of United States adults. *Am J Respir Crit Care Med* 2001;**164**:372–7.
36. Birring SS, Brightling CE, Bradding P, Entwisle JJ, Vara DD, Grigg J. Clinical, radiologic, and induced sputum features of chronic obstructive pulmonary disease in nonsmokers. a descriptive study. *Am J Respir Crit Care Med* 2002;**166**:1078–83.
37. Miravitlles M, Ferrer M, Pont A, Viejo JL, Masa JF, Gabriel R, et al. Characteristics of a population of COPD patients identified from a population-based study. Focus on previous diagnosis and never smokers. *Respir Med* 2005;**99**:985–95.

38. Behrendt CE. Mild and moderate-to-severe COPD in non-smokers. Distinct demographic profiles. *Chest* 2005;**128**: 1239–44.
39. Pauwels RA, Buist AS, Calverley PMA, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO global initiative for chronic obstructive lung disease (GOLD) workshop summary. *Am J Respir Crit Care Med* 2001;**163**: 1256–76.
40. Celli BR, MacNee W. and committee members. standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J* 2004;**23**:932–46.